

detecting, imaging, and treating of tumors; tomographic imaging of organs; monitoring of organ functions; performing coronary angiography, fluorescence endoscopy, laser guided surgery; and performing photoacoustic and sonofluorescent methods.

5 Specific embodiments to accomplish some of the aforementioned biomedical applications are given below. The inventive dyes are prepared according the methods well known in the art.

In two embodiments, the inventive bioconjugates have the formulas 1 or 2 where  $W_1$  and  $W_2$  may be the same or different and are  
 10 selected from the group consisting of  $-C(CH_3)_2$ ,  $-C((CH_2)_aOH)CH_3$ ,  $-C((CH_2)_aOH)_2$ ,  $-C((CH_2)_aCO_2H)CH_3$ ,  $-C((CH_2)_aCO_2H)_2$ ,  $-C((CH_2)_aNH_2)CH_3$ ,  $-C((CH_2)_aNH_2)_2$ ,  $-C((CH_2)_aNR^{12}R^{13})_2$ ,  $-NR^{12}$ , and  $-S-$ ;  $Y_1$  and  $Y_2$  are selected from the group consisting of hydrogen, tumor-specific agents,  $-CONH-Bm$ ,  $-NHCO-Bm$ ,  $-(CH_2)_a-CONH-Bm$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-CONH-Bm$ ,  $-(CH_2)_a-NHCO-Bm$ ,  
 15  $-CH_2-(CH_2OCH_2)_b-CH_2-NHCO-Bm$ ,  $-(CH_2)_a-NR^{12}R^{13}$ , and  $-CH_2(CH_2OCH_2)_b-CH_2NR^{12}R^{13}$ ;  $Z_1$  and  $Z_2$  are independently selected from the group consisting of hydrogen, phototherapy agents,  $-CONH-Dm$ ,  $-NHCO-Dm$ ,  $-(CH_2)_a-CONH-Dm$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-CONH-Dm$ ,  $-(CH_2)_a-NHCO-Dm$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-NHCO-Dm$ ,  $-(CH_2)_a-NR^{12}R^{13}$ , and  $-CH_2(CH_2OCH_2)_b-CH_2NR^{12}R^{13}$ ;  $K_1$  and  $K_2$  are  
 20 independently selected from the group consisting of  $C_1-C_{10}$  alkyl,  $C_5-C_{20}$  aryl,  $C_1-C_{20}$  alkoxy,  $C_1-C_{20}$  aminoalkyl,  $-(CH_2)_a-CO-$ ,  $-(CH_2)_a-CONH$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-CONH-$ ,  $-(CH_2)_a-NHCO-$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-NHCO-$ , and  $-CH_2-(CH_2OCH_2)_b-CO-$ ;  $X_1$  and  $X_2$  are single bonds, or are independently selected from the group consisting of nitrogen,  $-CR^{14}-$ ,  $-CR^{14}R^{15}$ , and  $-NR^{16}R^{17}$ ;  $Q$  is a  
 25 single bond or is selected from the group consisting of  $-O-$ ,  $-S-$ , and  $-NR^{18}$ ;  $a_1$

and  $b_1$  independently vary from 0 to 3;  $B_m$  is selected from the group consisting of bioactive peptides containing 2 to 30 amino acid units, proteins, antibody fragments, mono- and oligosaccharides;  $D_m$  is selected from the group consisting of photosensitizers, photoactive molecules, and phototherapy agents;  $a$  and  $c$  independently vary from 1 to 20; and  $b$  and  $d$  independently vary from 1 to 100.

In two other embodiment, the bioconjugates according to the present invention have the formulas 3 or 4 wherein  $W_1$  and  $W_2$  may be the same or different and are selected from the group consisting of  $-(CH_3)_2$ ,  $-C((CH_2)_aOH)CH_3$ ,  $-C((CH_2)_aOH)_2$ ,  $-C((CH_2)_aCO_2H)CH_3$ ,  $-C((CH_2)_aCO_2H)_2$ ,  $-C((CH_2)_aNH_2)CH_3$ ,  $-C((CH_2)_aNH_2)_2$ ,  $-C((CH_2)_aNR^{12}R^{13})_2$ ,  $-NR^{12}$ , and  $-S$ ;  $Y_1$  and  $Y_2$  are selected from the group consisting of hydrogen, tumor-specific agents,  $-CONH-B_m$ ,  $-NHCO-B_m$ ,  $-(CH_2)_a-CONH-B_m$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-CONH-B_m$ ,  $-(CH_2)_a-NHCO-B_m$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-NHCO-B_m$ ,  $-(CH_2)_a-NR^{12}R^{13}$ , and  $-CH_2(CH_2OCH_2)_b-CH_2NR^{12}R^{13}$ ;  $Z_1$  and  $Z_2$  are independently selected from the group consisting of hydrogen, phototherapy agents,  $-CONH-D_m$ ,  $-NHCO-D_m$ ,  $-(CH_2)_a-CONH-D_m$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-CONH-D_m$ ,  $-(CH_2)_a-NHCO-D_m$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-NHCO-D_m$ ,  $-(CH_2)_a-NR^{12}R^{13}$ , and  $-CH_2(CH_2OCH_2)_b-CH_2NR^{12}R^{13}$ ;  $K_1$  and  $K_2$  are independently selected from the group consisting of  $C_1-C_{10}$  alkyl,  $C_5-C_{20}$  aryl,  $C_1-C_{20}$  alkoxy,  $C_1-C_{20}$  aminoalkyl,  $-(CH_2)_a-CO-$ ,  $-(CH_2)_a-CONH-$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-CONH-$ ,  $-(CH_2)_a-NHCO-$ ,  $-CH_2-(CH_2OCH_2)_b-CH_2-NHCO-$ , and  $-CH_2-(CH_2OCH_2)_b-CO-$ ;  $X_1$  and  $X_2$  are single bonds or are independently selected from the group consisting of nitrogen,  $-CR^{14}$ ,  $-CR^{14}R^{15}$ , and  $-NR^{16}R^{17}$ ;  $A_1$  is a single or a double bond;  $B_1$ ,  $C_1$ , and  $D_1$  are independently selected from the group consisting of  $-O-$ ,  $-S$ ,  $-CR^{11}$ , alkyl,  $NR^{12}$ , and  $-C=O$ ;  $A_1$ ,

B<sub>1</sub>, C<sub>1</sub>, and D<sub>1</sub> may together form a 6- to 12-membered carbocyclic ring or a 6- to 12-membered heterocyclic ring optionally containing one or more oxygen, nitrogen, or sulfur atoms; a<sub>1</sub> and b<sub>1</sub> independently vary from 0 to 3; B<sub>m</sub> is selected from the group consisting of bioactive peptides containing 2 to 30 amino acid units, proteins, antibody fragments, mono- and oligosaccharides; bioactive peptides, protein, and oligosaccharide; D<sub>m</sub> is selected from the group consisting of photosensitizers, photoactive molecules, and phototherapy agents; a and c independently vary from 1 to 20; and b and d independently vary from 1 to 100.

10 In one embodiment of the invention, the dye-biomolecule conjugates are useful for optical tomographic, endoscopic, photoacoustic and sonofluorescent applications for the detection and treatment of tumors and other abnormalities. These methods use light of wavelengths in the region of 300-1300 nm. For example, optical coherence tomography (OCT), also  
15 referred to as "optical biopsy," is an optical imaging technique that allows high resolution cross sectional imaging of tissue microstructure. OCT methods use wavelengths of about 1280 nm.

In various aspects of the invention, the dye-biomolecule conjugates are useful for localized therapy for the detection of the presence or  
20 absence of tumors and other pathologic tissues by monitoring the blood clearance profile of the conjugates, for laser assisted guided surgery (LAGS) for the detection and treatment of small micrometastases of tumors, e.g., somatostatin subtype 2 (SST-2) positive tumors, upon laparoscopy, and for diagnosis of atherosclerotic plaques and blood clots.